REMARKS

Claims 85 and 86 are pending in the application.

- Claims 85 and 86 are newly objected to.
- Claims 85 and 86 are newly rejected under 35 USC, 112, first paragraph as being non-enabled.
- Claims 85 and 86 are rejected under 35 USC 102(b) as being anticipated by Cordell as evidenced by a reference from the Australian Proteome Analysis Facility, submitted as Exhibit A in Remarks filed 6/13/2008 and Crowther (ELISA: Theory and Practice: Methods in Molecular Biology, 42, Humana Press, Totowa, NJ, May 1, 1995).
- The previously pending rejection of Claims 85 and 86 under 35 USC 102(a) as being anticipated by Schenk, et al. (WO 99/27944) as evidenced by a reference from the Australian Proteome Analysis Facility, submitted as Exhibit A in Remarks filed 6/13/2008 has been withdrawn.
- The previously pending rejection of Claims 85 and 86 under 35 USC 103(a) as being unpatentable over Wong, et al., PNAS, 82:8729 – 8732 (1985), in view of Schenk, et al, has been withdrawn.

Amendments to the Claims

Claims 85 and 86 have been amended to clarify the features of the pending invention. Claim 85 has been amended by moving the limitation of "in the presence of physiological levels of human serum albumin" from step d) of the claim to step b) of the claim. Claim 86 has been amended by moving the limitation of "in the presence of 60 mg/ml human serum albumin" from step d) of the claim to step b) of the claim. The amendments add no new matter to the specification.

Objection of Clams 85 and 86

Claims 85 and 86 are newly objected to for containing periods between "NO" and ":". The claims have been amended consistent with the Examiner's remarks. In view of the amendments, withdrawal of the objection is respectfully requested.

Rejection under 35 USC, 112, Enablement

Claims 85 and 86 are newly rejected under 35 USC, 112, first paragraph as being non-enabled. The Applicant respectively traverses this rejection.

The claims are rejected for not being enabled for a method wherein steps (a) through (c) of the claim occur *in vivo*. However, the methods of Claims 85 and 86 do not necessarily require that steps (a) through (c) of the claimed method be performed *in vivo*. Claim 85 requires that steps (a) through (c) be performed " in the presence of physiological levels of human serum albumin" and Claim 86 requires that steps (a) through (c) be performed albumin "in the presence of 60 mg/ml human serum albumin." Even though the present claims are not required to be performed *in* vivo one of ordinary skill in the art would be able to do so based on the teachings provided by the pending specification and the knowledge of one of ordinary skill in the art.

The Patent Office makes the assertion that a clinical trial would need to be performed to show enablement of the present invention. Pending Action, page 7. As indicated in the MPEP, no such "clinical trial" is necessary to show enablement of an invention. Rather, a reasonable correlation between *in vitro* and *in vivo* model systems and the claimed invention, in the context of the knowledge of one of ordinary skill in the art, is all that is required. MPEP, 2164.02. The present specification provides such *in vitro* and *in vivo* support for the claimed invention. The exemplification at least at ¶ [0075] and Table 4 of the pending specification provide *in vitro* support for the present invention. The exemplification at least at ¶ [0087] – [0088] and Table 7 of the pending specification provide *in vivo* support of the present invention in a murine model system. While the Patent Office makes the assertion that murine model systems are not adequate as a correlative model system for humans due to a lower level of serum, the Applicant submits that when the exemplification in the specification is taken as a whole, and not attacked individually as the Patent Office has done, the *in* vitro and *in* vivo exemplification provided by the specification provides one of ordinary skill in the art the ability to perform the claimed invention without undue experimentation.

The Patent Office then goes on to admit that steps a) – c) were within the ability of one of skill in the art at the time of the filing of the instant application by reference to a previously cited Schenk reference (WO 99/27944) that is not prior to the instant invention.

Nevertheless, the specification in combination with what was known in the art at the time of filing does provide support for steps (a) through (c) of method of Claims 85 and 86 to be performed *in vivo*. The teachings of Schenk WO 99/27994, while not prior art to the present invention for reasons presented in the response paper filed with the Patent Office on December

22, 2010, were known in the art at the time of filing of the present invention. As stated in the Office Action dated 7/30/2010 at ¶ 21 with regard to the then pending 102(a) anticipation rejection:

> 21. The Schenk et al. WO publication discloses methods comprising administering an antigenic epitope of beta-amyloid *in vivo* to induce the formation of an immune response and detecting the resultant antibody-antigen immune complexes. Specifically, the Schenk publication teaches generating immune complexes against beta amyloid or fragments thereof (residues 1-5; 1-12; 13-28; and 1-40) *in vivo*. Thus, since the epitopes as disclosed by Schenk et al. fully encompass residues 9-25 (SEQ ID NO: 3) of beta-amyloid, and barring evidence within the instant disclosure as to specific residues to which the antibody of the instant claims binds (i.e. epitope mapping), then the antibodies of the Schenk prior art anticipate the "an antibody generated to the central region" as required by the invention. Additionally, since the immune response is generated *in vivo*, then the method as taught by Schenk occurs in the presence of physiological levels of serum albumin. And since the Schenk disclosure explicitly contemplates the method as performed in humans (page 12 lines 25-27), immune complexes formed in the presence of 60 mg/ml of human serum albumin are anticipated. Lastly, the Schenk et al. reference teaches removing a blood sample from immunized subjects and detecting the serum antibody titers specific for these beta-amyloid central antigens (pages 54-55 and Figs. 13 and 14). Thus, the methods of the instant claims fails to distinguish over that disclosed within the prior art.

Art cited in an anticipation rejection must be enabled.

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... ." MPEP 2121.01. *In re Hoeksema,* 399 F.2d 269, 158 USPQ 596 (CCPA 1968).

and,

> The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. MPEP 2121.01. *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003).

Thus, that the Patent Office cited the Schenk reference as an anticipatory reference the Patent Office has already admitted to the enablement of the cited reference and, by extension, the presently claimed invention.

Schenk, although not considered prior art to the present invention for the reasons given in the response dated 12/22/2010 and as acknowledged by the Patent Office in the presently pending Office Action, was known at the time of filing of the present invention. In the presently pending Office Action, the Patent Office states that Schenk "do not explicitly teach or suggest the removal of a sample to detect the immune complex of amyloid beta and an antibody raised against the central portion, as required by step (d) of the instant claims. " Pending Action, page 5. First, this statement is contrary to the arguments made by the Patent Office in the Action dated 7/30/2010 where it is stated: "Lastly, the Schenk et al. reference teaches removing a blood sample from immunized subjects and detecting the serum antibody titers specific for these beta-amyloid central antigens (pages 54-55 and Figs. 13 and 14)." However, with regard to step d) and while not necessarily acquiescing to the remarks made by the Patent Office, Claims 85 and 86 have been amended as indicated above rendering this portion of the enablement rejection moot.

Rejection under USC 35, 102(b)

Claims 85 and 86 are newly rejected under 35 USC 102(b) as being anticipated by Cordell as evidenced by a reference from the Australian Proteome Analysis Facility, submitted as Exhibit A in Remarks filed 6/13/2008 and Crowther, ELISA, Theory and practice, Methods in Molecular Biology 42, Humana Press, Totowa, NJ, May 1, 1995. The Applicant respectively traverses this rejection.

The Examiner states Cordell teaches "an in vitro method of diagnosing familial amyloidosis or Alzheimer's disease comprising providing a serum sample from a patient which contains circulating beta-amyloid in the presence of human serum albumin from a patient … treating said sample to a "panel of beta-amyloid antibodies" and then analyzing the samples "using solid-phase ELISA techniques." Pending Action, pages 4 and 5.

For a reference to be anticipatory it must teach explicitly or inherently each element of the claimed invention. MPEP, 2131. Cordell does not meet this standard. The present invention requires the formation of an immune complex in the presence of physiological levels of human serum albumin (or 60 mg/ml of human serum albumin). However, and unlike the present invention, the Patent Office has not shown that Cordell teaches this limitation. Rather, Cordell teaches immunological complexes being made in "solid-phase ELISA assays" and not in

the presence of physiological levels of human serum albumin. ELISA assays typically require the dilution of the sample to be tested by 1:100 to 1:10,000. Thus, the concentration of serum albumin in the ELISA cannot be in the presence of physiological (or 60 mg/ml) of human serum albumin, as is presently claimed. Further, the Patent Office can not read into Cordell the limitation of an immune complex being formed in the presence of physiological levels of human serum or 60 mg/ml of human serum just because the reference does not explicitly exclude this possibility, especially when the proffered supportive reference (Crowther: see, below) teaches away from this very limitation. Thus, Cordell can not be anticipatory to the presently claimed invention.

The Patent Office supplements the teachings of Cordell with Crowther. Crowther is cited as teaching "whole serum can be used in solid phase ELISA (see page 169)." Pending Action, page 11. However, Crowther does not actually teach this. Rather, Crowther teaches that the use of whole serum "is not recommended" because Ig cannot be measured because it is contaminated with "serum proteins that compete for plastic binding sites preferentially over IgG." Crowther, page 169. In other words, a complete reading of Crowther, in context, teaches that *the use of whole serum is not a viable option* for a solid phase ELISA assay. Crowther then teaches a method wherein whole serum is diluted "at 1/100" with subsequent twofold dilutions. Crowther, page 170. Thus, Crowther does not provide the teachings necessary to render Cordell an anticipatory reference. In fact, this teaching by Crowther meets the standard of teaching away as discussed in *In re* Fulton where it is stated that a prior art reference teaches away if it serves to "criticize, discredit, or otherwise discourage the solution claimed…." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). MPEP § 2141.02, VI. Crowther criticizes, discredits and otherwise discourages the use of whole serum in an ELISA assay and, when taken as a supportive reference for Cordell, likewise serves to criticize, discredit and otherwise discourage the use of whole serum in an ELISA assay in the context of the teachings of Cordell.

Therefore, the Patent Office has failed to make an anticipatory showing of an immune complex formed between beta-amyloid and an antibody generated to the central region of beta-amyloid in the presence of physiological levels of human serum albumin or 60 mg/ml of human serum albumin.

In view of the proffered remarks, the Applicant respectfully requites that the pending rejection be withdrawn.

Summary

In light of the above amendment and attendant remarks, consideration of the subject patent application is respectfully requested. If an interview would be beneficial to the prosecution of this case, Applicants respectfully request that Examiner MacFarlane contact the representatives of record. Any deficiency or overpayment should be charged or credited to Deposit Account No. 50-4514. Applicants note that new rejections proffered by the Examiner appear redundant in view of previously withdrawn rejections. This is contrary to the compact prosecution required by the USPTO [MPEP 2106, II]. Applicants respectfully request withdrawal of the pending rejections and allowance of the claims.

Respectfully submitted,

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